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Endoscopic treatment for chronic pancreatitis: indications, technique, results

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Abstract Endoscopic treatment associated with or without extracorporeal shock wave lithotripsy (ESWL) for chronic pancreatitis has been employed for about 20 years. Although two randomized control trials have revealed the greater effectiveness of surgery as compared to endoscopic treatment for chronic pancreatitis, a considerable number of patients have successfully obtained complete and long-term relief from pain by the less invasive endoscopic treatment. In this review, we discuss the indications, techniques and results of endoscopic treatment and ESWL for painful chronic pancreatitis. We also discuss the characteristic clinical features that are predictive of a good response to endoscopic treatment and ESWL.

Keywords Chronic pancreatitis · Endoscopic treatment · ESWL · Stent · Endoscopic

Introduction

Chronic pancreatitis (CP) is an inflammatory disease in which progressive and irreversible structural changes to the pancreas result in a permanent impairment of both the exocrine and endocrine function [1]. Pain is a predominant symptom of CP, which often requires treatment, and its origin is multifactorial [2]. Pancreatic tissue hypertension due to duct obstruction by pancreatic stones (Fig. 1a) and/or strictures (Fig. 1h) have been suggested as causes of the pain. Therefore, pancreatic duct drainage has been proposed as an effective treatment for painful CP [1].

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The endoscopic approach combined with extracorporeal shock wave lithotripsy (ESWL) to decompress the pancreatic duct has become a widespread therapy for patients with painful CP. Once established, the nature of CP is progressive and irreversible and there is no effective therapy that can completely cure patients with advanced CP. Because the goal of treatment is to relieve the symptoms rather than cure the disease itself [1], the therapy should be elected from the standpoint of safety and low degree of invasiveness [3]. From this point of view, because of its lower invasiveness, endoscopic treatment for painful CP may be preferred, with surgery reserved as a second-line therapy [3].

Recently, two randomized control trials have been published [4, 5]. One demonstrated the greater effectiveness of surgery as compared to endoscopic treatment, which, however, did not include ESWL in the treatment protocol, for long-term pain reduction, while there was no difference in the short-term results between these two therapies [4]. The authors suggested the endoscopic treatment could be offered as a first-line treatment, with surgery being performed in case of failure and/or recurrence [4]. The other study described that patients assigned to surgical drainage, as compared with patients assigned to endoscopic treatment, had lower Izbicki pain scores and better physical health summary scores at the end of a 2-year follow-up [5]. Although these data clearly showed surgery was more effective than endoscopic treatment, the patients registered in this study tended to have advanced CP with exocrine insufficiency and 84% of them had dominant strictures in the pancreatic duct [5], which might have been responsible for the unsatisfactory result of the endoscopic treatment. The indications for endoscopic treatment should be determined precisely. Here we discuss the indications, techniques and results of endoscopic treatment for painful CP

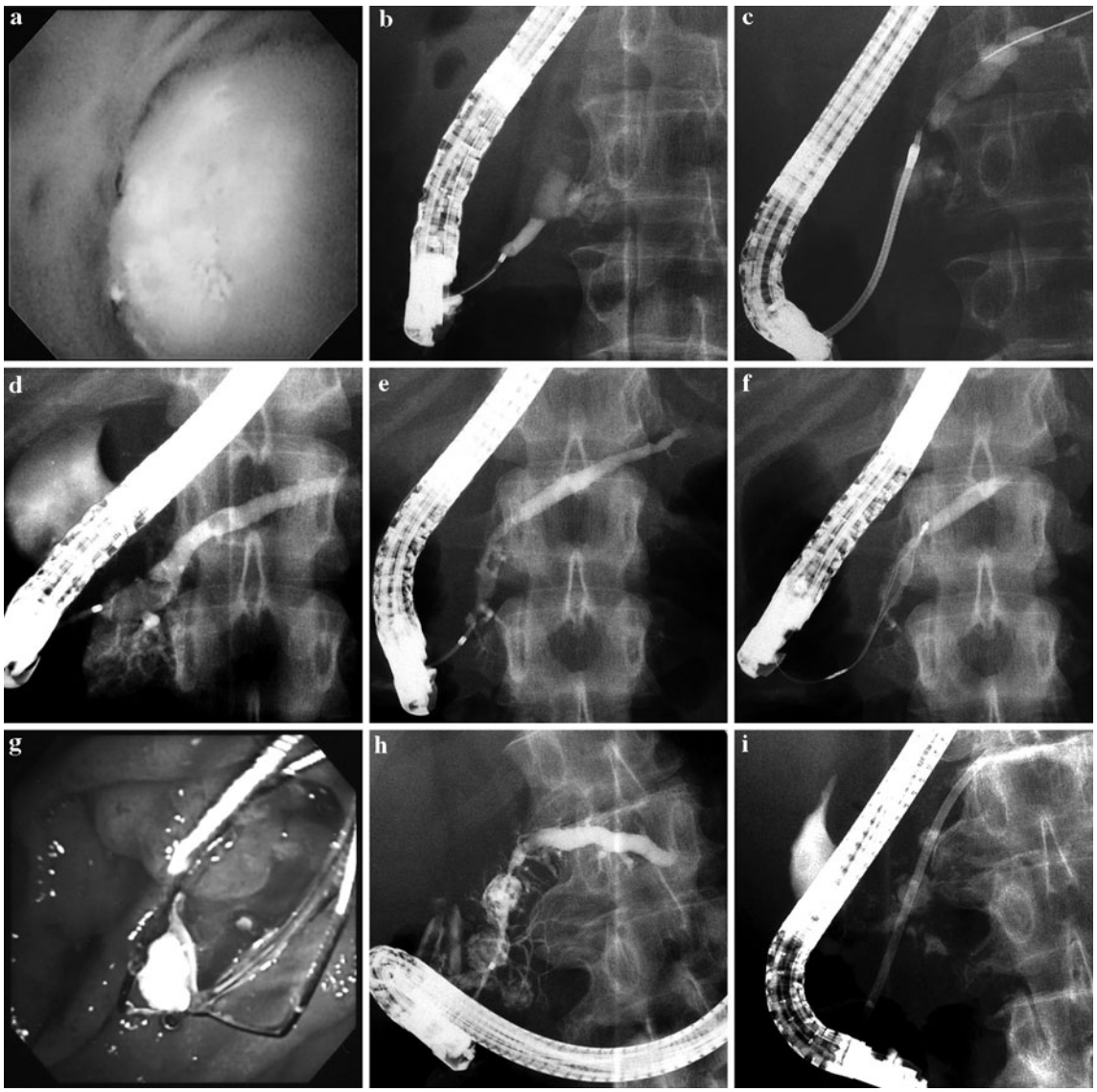

Fig. 1 **a** A pancreatic stone in main pancreatic duct visualized by POPS. **b** A pancreatic stone impacting and sticking to the pancreatic duct. **c** Soehendra stent retriever drilled and passed through the pancreatic stone. **d** A pancreatic stone impacting behind a stricture of the main pancreatic duct, in another case. **e** After ESWL sessions, the stone was fragmented. **f**, **g** The fragmented stones were successfully removed by endoscopic treatment. **h** Another case of chronic pancreatitis with duct strictures. **i** The patient required pancreatic stent placement bridging the strictures

to devise a better therapeutic strategy on the basis of appropriate selection between the endoscopic or the surgical approach.

Indications

Endoscopic treatment for CP focuses on pain. Ductal obstruction and resulting tissue hypertension plays a major role, mainly by inducing ischemia and the resulting inflammatory cascade [6]. The purpose of endoscopic treatment is to decompress tissue hypertension by stone removal, ESWL and/or stent placement across strictures of the pancreatic duct. CP patients with pain due to suspicious ductal hypertension are considered candidates for endoscopic treatment.

Because it is sometimes hard to distinguish the patients who have symptoms or findings suggestive of chronic pancreatitis from those who in fact have pancreatic cancer [1, 7], it should be emphasized that appropriate imaging tests, including contrast enhancing computed tomography (CECT), magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP), are usually required to distinguish pancreatic cancer from other suspicious cases.

Endoscopic brush-cytology and EUS imaging with fine-needle aspiration biopsy can also confirm cancer [7].

Patients with stones situated in a dilated pancreatic duct without strictures, stones behind soft strictures or stones associated with pancreas divisum are eligible for endoscopic treatment with ESWL [8]. Patients with distal strictures and upstream dilatations of the pancreatic duct are good candidates for pancreatic stenting [9]. In contrast, patients with strictures or stones situated in a body/tail lesion do not respond as well to endoscopic treatment as to ESWL [8, 10]. Patients with a concomitant fluid collection, an elevated alkaline phosphatase suggestive of biliary obstruction, with a huge stone burden, multiple side branch calcifications or active cholangitis are not considered a eligible for ESWL [11].

Technique

Patients with pancreatic intraductal stones have been successfully treated by combining ESWL and endoscopic techniques for pancreatic sphincterotomy, stone removal, stricture dilatation and stent placement. Pancreatic stones tend to be multiple, hard and spiculed and they are usually stuck to the ductal epithelium (Fig. 1b) or impacted behind ductal strictures (Fig. 1d). ESWL is the best technique to fragment the stones before removal as compared to mechanical lithotripsy and electrohydraulic lithotripsy, which have limited indications [8].

Pancreatic sphincterotomy (5–6 mm) is a basic technique for improving access to the pancreatic duct, which is oriented at 13 h and limited to the ampullary bulge. It employs a pure cutting current or an endocut mode in a single step procedure or after biliary sphincterotomy [8, 12]. Minor papilla sphincterotomy can also be done if necessary. Then, devices for removing pancreatic stones or dilating strictures are able to access the duct over a hydrophilic 0.035- or 0.025-in. guide wire. If the guide wire cannot pass beyond the duct stricture or impacting stones (Fig. 1b, d) in pancreatic head lesions, ESWL can be begun without doing pancreatic sphincterotomy and/or stenting [13–15]. In patients who have radiolucent stones, a pancreatic sphincterotomy and placement of a nasopancreatic catheter before the ESWL are sometimes required [8]). After fragmentation of the ductal stones (Fig. 1e), ERCP is then performed with the aim of perfect clearance of the pancreatic stones. Fragments of stones are cleared endoscopically through a pancreatic sphincterotomy using a basket (Fig. 1f, g) or an extractor-balloon. On average, patients with multiple pancreatic stones require around two to three sessions of ESWL and around three to four sessions of endoscopic treatment for complete clearance. This can usually be achieved in 1 year, with follow-up examination and procedures at 3-month intervals [8].

In cases with a dominant pancreatic duct stricture (Fig. 1h), duct dilatation with a balloon or dilatator is required to place a stent bridging the stenosis (Fig. 1i). In fact, the stricture is usually tight because of expansive fibrosis and hard, impacted stones. A Soehendra stent retriever is useful for dilating hard strictures and for drilling holes in the stones [16] (Fig. 1c). After dilatation, a stent with an adequate diameter (5–10 Fr) and length is usually required to bridge the stricture. It has been suggested that 100% polyethylene stents (5–7 Fr) will occlude if they are left in place for more than 9 weeks [17]). Therefore, the stents may need to be removed within 9 weeks to avoid the risk of complications by stent occlusion, such as pancreatitis or infection. If a significant stricture persists at the time of stent removal, the stent needs to be replaced, and sequential exchange is sometimes required. It has also been suggested that clogging of the pancreatic stent alone is rarely associated with clinical symptoms because the pancreatic juice tends to drain from the side of the obstructed stent [8]. In fact, it has been demonstrated that it takes around 6–12 months on average for clinical symptoms such as a pain to emerge after continuous single stent placement [18, 19]. The optimum stent exchange interval is not currently known. We usually exchange stents every 3 months while others have reported intervals of from 2 to 12 months [4, 5, 20–23] or according to an on demand policy [18, 19].

Because fibrous duct strictures are sometimes resistant to endoscopic therapy, they can persist after stent removal and cause pain relapse in some patients. The placement of multiple stents in the pancreatic duct has been proposed [24]. The mean number of stents placed through the major or minor papilla was 3. The duration of stent placement was from 6 to 12 months, and 84% of the patients were asymptomatic during a mean follow-up of 38 months after stent removal [24]. Self-expandable metal stents have also been tested [25]. Against expectation, the trial results were unsatisfactory due to frequent stent occlusion by mucosal hyperplasia during the follow-up [25].

Results

Short-term results

Endoscopic treatment for CP was technically successful in 54–100% of cases and most studies reported more than 85% technical success [4, 5, 13, 18, 20–22, 26–34]. Complete removal of pancreatic stones in the main pancreatic duct was obtained in 42–100 of the cases [13, 26–28, 30–34], with most reports showing between 50 and 70%. The short-term clinical results showed immediate improvement of pain in 50–100% of the cases (Table 1).

Table 1 Improvement of pain

	Treatment	*n*	Immediate (%)	During follow-up (complete relief) (%)	Follow-up (year)	Surgery (%)	Complication (%)	Mortality (%)	Reference
Sauerbruch	ESWL + endoscopic (without stent)	8	50	50 (37)	0.9 (0.2–2.2)	0	13	0	Sauerbruch et al. [26]
Sauerbruch	ESWL + endoscopic (without stent)	24	–	83 (50)	2.0 (0.3–4.6)	8	8	0	Sauerbruch et al. [27]
Dumonceau	ESWL + endoscopic (without stent)	63	95	54 (54)	2.0 (mean)	6	13	0	Dumonceau et al. [28]
Inui	ESWL + endoscopic (without stent)	555	91	–	3.7 (0.3–11.8)	4	6	0.2	Inui et al. [14]
Ohara	ESWL	32	–	96 (79)	3.7 (1.3–5.3)	3	16	0	Ohara et al. [13]
Dumonceau	ESWL	26	–	58 (58)	4.3 (mean)	4	0	0	Dumonceau et al. [15]
Grimm	ESWL + endoscopic (with stent)	70	82	57	1.6 (0.2–3)	20	33	3	Grimm et al. [29]
Cremer	ESWL + endoscopic (with stent)	75	94	85	3.1 (1.5–6)	15	16	0	Cremer et al. [18]
Delhaye	ESWL + endoscopic (with stent)	123	–	85 (45)	1.2 (mean)	8	34	0	Delhaye et al. [30]
Schneider	ESWL + endoscopic (with stent)	50	82	90 (62)	1.7 (0.2–4.2)	12	14	0	Schneider et al. [31]
Binmoeller	ESWL + endoscopic (with stent)	93	74	65	4.9 (mean)	26	6	0	Binmoeller et al. [19]
Smiths	ESWL + endoscopic (with stent)	53	–	79	2.8 (0.3–10.9)	15	9	0	Smits et al. [32]
Adamek	ESWL + endoscopic (with stent)	80	–	76	3.3 (2–7.7)	10	3	0	Adamek et al. [22]
Rosch	ESWL + endoscopic (with stent)	1018	88	86 (66)	4.9 (2–12)	24	13	–	Rosch et al. [10]
Delhaye	ESWL + endoscopic (with stent)	56	85	66	14.4 (mean)	21	25	0	Delhaye et al. [33]
Gabbrielli	ESWL + endoscopic (with stent)	22	100	27 (27)	6.0 (1–13.5)	18	9	0	Gabbrielli et al. [34]
Cahen	ESWL + endoscopic (with stent)	19	–	32 (16)	2.0	21	58	5	Cahen et al. [5]
Dumonceau	ESWL + endoscopic (with stent)	29	–	55 (55)	4.3 (mean)	10	3	0	Dumonceau et al. [15]
Smiths	Stent	49	82	78 (24)	2.8 (0.5–10.7)	12	18	0	Smith et al. [21]
Ponchon	Stent	23	74	52 (52)	1.0	13	–	0	Ponchon et al. [20]
Morgan	Stent	25	65	–	–	–	–	–	Morgan et al. [23]
Dite	Stent	64	92	65 (14)	5.0	–	8	0	Dite et al. [4]

Long-term results

Long-term improvement of pain during the follow-up was obtained variously in 27–96% of the cases (Table 1). The follow-up periods (0.9–14.4 years) were also various. Complete pain relief at the end of the follow-up was obtained in 14–79% of the cases. A meta-analysis demonstrated that the mean effect size (weighted correlation coefficient) for pain by ESWL and/or endoscopic treatments in chronic pancreatitis was 0.6215 [35]. A large-

scale cohort study ($n = 1018$, follow-up period with a mean of 4.9 years) demonstrated that 66% of the patients showed a good clinical course without pain during the follow-up period [10]. Another study demonstrated that, even after long follow-up periods with a mean of 14.4 years, long-term clinical success was obtained in 66% (37/56) of the patients [33]. In the majority of the reports, it was reported that 10–20% of patients underwent surgery during the follow-up periods due resistance to the endoscopic therapy (Table 1).

Complications

Complications related to ESWL or endoscopic treatments have been reported. Mild pancreatitis, bleeding after pancreatic sphincterotomy, stent clogging and infections were complications that sometimes occurred. Frequencies of from 0 to 58% were reported (Table 1). Mortalities related to the procedure have rarely been reported (Table 1).

Short duration of chronic pancreatitis seems to promise good response

One of the factors that may facilitate a good clinical outcome after ESWL and/or endoscopic treatments is a short duration of disease before the initial therapy [19, 28, 33]. Binmoeller et al. [19] demonstrated that the patients who did not respond to treatment were found to have a history of symptomatic chronic pancreatitis that was nearly twice as long as that of the patients who responded (7.0 vs. 4.1 years, respectively). Moreover, Delhaye et al. [33] demonstrated that the absence of ongoing smoking and shorter duration (4 ± 3 years) of disease before treatment were independent predictive factors for clinical success.

The obstinance of strictures as a factor

Strictures of the pancreatic duct could be successfully treated by pancreatic stent insertions with technical success in 85–99% of the cases [4, 18, 20, 21]. Immediate clinical success also was obtained in 65–92% of patients by stent placement bridging the stricture [4, 18, 20, 21]. Although these results are thought to be satisfactory, a serious problem is that the disappearance of the stricture was not frequently observed after stent removal. The persistence of ductal strictures was found in more than half of the patients [5, 18, 20]. The stents had to be exchanged sequentially in many patients because of such persistent strictures. Obstinate duct strictures were found in 25–59% of patients [18, 19, 21, 29, 33]. Moreover, even when the strictures seemed to improve, 19–38% of the patients required re-stenting after attempting to remove a stent because of recurrent symptoms [19, 21, 36]. Stent-related complications such as stent clogging were found in 25–55% of the patients [5, 21, 32]. In many cases, pancreatic stent therapy required repeated endoscopic procedures increasing the cost and number of hospital stays. On the other hand, a portion of patients (14–52%: Table 1) with duct strictures improved after stent therapy and obtained long-term clinical success with complete pain relief. Even though pancreatic duct strictures are refractory to endoscopic treatment, it is a great advantage for some patients to be able to avoid surgery by temporary pancreatic stenting.

ESWL alone may be a good and economical alternative

Ohara et al. [13] reported that a single application of ESWL was an acceptable therapy with good long-term results for patients with pancreatic duct stones (Table 1). Recently, Dumonceau et al. [15] reported a randomized control trial comparing the therapeutic results of ESWL alone with ESWL combined with endoscopic therapy for painful chronic pancreatitis. The clinical successes were comparable while treatment costs were three times higher in the ESWL combined with endoscopy group as compared with the ESWL alone group [15]. In this paper, the authors described that obstructive calcification in the head of the pancreas was the only single factor that was independently associated with pain relapse [15].

Conclusion

What are the characteristic clinical features predictive of clinical success by endoscopic treatment?

1. Short duration of symptomatic CP (<4 year).
2. The absence of pancreatic duct stricture.
3. Obstructive calcifications restricted to the pancreas head.

Endoscopic treatment and/or ESWL is strongly recommended for patients satisfying the above criteria. Surgery can be elected for patients who do not satisfy the above criteria without attempting the endoscopic approach. However, it is noted that even if a patient does not satisfy the above criteria, there is a possibility of benefitting from endoscopic treatment and/or ESWL. Endoscopic treatment and/or ESWL can be regarded as a first-line therapy because of its low degree of invasiveness. As surgical treatment is superior for long-term pain reduction, it can be considered when repeated endoscopic treatment fails. The economic benefits of endoscopic therapy as compared to surgery remain to be evaluated.

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